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# Accepted Manuscript

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## Mood-congruent recollection and anosognosia in Alzheimer's Disease

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**ABSTRACT**

The aim of the study was to investigate experimentally the impact of current mood state on anosognosia or awareness of symptoms in AD patients, in which mood state was manipulated by giving tasks that were either easy (success condition) or very difficult (failure condition). Twenty-two patients with mild to moderate AD participated. Four success-failure manipulation (SFM) computerized tasks were used as mood induction procedures, two based on reaction time tasks and the other on memory tasks. Level of awareness and the current mood state were assessed before and after each task, using a modified version of the Anosognosia Questionnaire for Dementia and a self-reported questionnaire respectively. For both types of task, the results indicate that the emotional state of the participants was similar before performing the tasks and that only the failure conditions induced a negative mood state. Additionally, regarding the level of awareness, there were no significant differences after the reaction time tasks but for the memory tasks, there was greater awareness of symptoms after performing the task in the failure condition. To the best of our knowledge, this study is the first exploring experimentally the impact of mood on anosognosia in AD. The results showed an improvement of awareness of symptoms after negative mood induction, but only when the task used in the SFM was memory-based.

Key words: dementia, Alzheimer's disease, awareness, anosognosia, mood

## 1. Introduction

Anosognosia refers to a lack of awareness about deficit or condition as found in various neurological conditions, such as aphasia, hemiplegia and also dementia (Mograbi, Brown, & Morris, 2009; Ries et al., 2007; Stuss, Rosenbaum, Malcolm, Christiana, & Keenan, 2005; Stuss, 1991). Unawareness regarding the disease or cognitive impairments is a common characteristic of Alzheimer's disease (AD) (Agnew & Morris, 1998; Morris & Hannesdottir, 2004), with estimates obtained with large samples reaching almost 80% (Antoine, Antoine, Guernonprez, & Frigard, 2004; Mograbi, Ferri, et al., 2012; Sousa et al., 2015). Lack of awareness has several important clinical implications (Bertrand, Landeira-Fernandez, & Mograbi, 2013; Spalletta, Girardi, Caltagirone, & Orfei, 2012), which go from diminished treatment adherence (Arlt, Lindner, Rösler, & Von Renteln-Kruse, 2008), increased engagement in high-risk situations (Seltzer, Vasterling, Yoder, & Thompson, 1997; Starkstein, Jorge, Mizrahi, Adrian, & Robinson, 2007), earlier institutionalization (Horning, Melrose, & Sultzer, 2014; Steele, Rovner, Chase, & Folstein, 1990) to increased caregiver burden (Clare et al., 2011; DeBettignies, Mahurin, & Pirozzolo, 1990; Rymer et al., 2002; Seltzer et al., 1997; Turró-Garriga et al., 2013).

The relationship with mood is an important aspect of anosognosia and has been explored using three main approaches (Mograbi and Morris, 2014). First, studies show mixed results when exploring awareness for different objects in dementia, with some findings suggesting that patients with AD present greater unawareness for cognitive deficits relative to behavioural changes (Kotler-Cope & Camp, 1995) and others results indicating also an "affective anosognosia" (Verhulsdonk, Quack, Höft, Lange-Asschenfeldt, & Supprian, 2013), that is, a lack of awareness for mood disturbance. Second, the literature suggests that people with AD may present an emotional response to failure situations even in the absence of explicit awareness. For

example, Mograbi, Brown, Salas and Morris (2012) showed that, in a failure situation, patients with AD exhibited the same emotional reactivity as did controls, despite unawareness of their performance. Third, when exploring the relation between level of awareness of deficits and the presence of depressive symptoms, numerous studies indicate that patients with AD who have a higher level of depression show more awareness or less anosognosia (Clare et al., 2012; Harwood, Sultzer, & Wheatley, 2000). Two possible explanations for these results can be found in the literature. On one hand, depressed patients may show “depressive realism” or present apparently more awareness because of a negative bias when reporting problems. On the other hand, increased awareness of difficulties might lead to higher depression, through a reactive depression process. Investigating the role played by emotional factors in anosognosia for hemiplegia, Besharati, Kopelman, Avesani, Moro and Fotopoulou (2015) showed that experimentally induced negative feelings improved awareness for motor deficits in anosognosic patients with right-hemisphere lesions. However, the question of a causal link between awareness and mood and the direction of this relationship still remains.

Another way to explore this link is through the well-known relationship between mood and memory. The most robust effects of mood on memory in the literature are the phenomena of mood-dependent memory (MDM) and mood-congruent memory (MCM). The former, as part of the global phenomenon of state-dependent memory, is improved memory for material when the subject’s mood is the same at the time of encoding and retrieval, this occurring independent of the material content (Bower, 1981; Eich & Metcalfe, 1989; Nutt & Lam, 2011). The latter refers to facilitated recovery of material when the emotional valence of this material is congruent with current mood (Bower, 1981). For example, when a person is currently in a positive mood state, the retrieval of positively toned material will be easier in comparison to the retrieval of negative

items. Most of the studies exploring MCM were conducted with young adults, but there are differential older adult effects. Specifically, Knight and Durbin (2015) reviewed studies with older adults and found a greater bias for recalling negative information when in a sad mood, compared to younger adults. Additionally, in a study including also AD participants, Fleming, Kim, Doo, Maguire, & Potkin (2003) demonstrated that AD patients remembered more negative items in an immediate recall memory task than neutral and positive words; healthy younger and older adults did not show this bias toward negatively toned material. The authors suggested the MCM effect as an explanation for these results. However, as current mood was not assessed, the data may not fully support their conclusions. Additionally, to the best of your knowledge, there is no published study exploring specifically the MDM and/or MCM effects in AD patients.

The aim of the current study was to investigate the impact of the current mood state on awareness of symptoms in AD patients, more specifically on the recollection of memories linked to their condition. For this purpose, we induced specific mood states using two experimental success-failure manipulation paradigms, one involving a reaction time task and the other a memory task. Participants were asked to answer questions regarding their condition before and after each mood manipulation. By using this method, we intended to explore not only the impact of mood on awareness but the additional influence of the context (memory vs. reaction time) on awareness as well. We hypothesized that the induction of a negative mood state would increase the retrieval of details regarding the patient's own deficits. However, we anticipated that the type of task would affect differentially the level of anosognosia, with a more marked increase of awareness after memory tasks in comparison to reaction time tasks.

## 2. Methodology

### 2.1. Participants

Twenty-four participants with mild to moderate AD (17 females) were recruited from the Center for Alzheimer's disease and Related Disorders (CDA) of the Institute of Psychiatry of the Federal University of Rio de Janeiro (IPUB-UFRJ), Brazil. The clinical diagnosis of AD was made by a psychiatrist using clinical interviews with the patients and caregivers, cognitive screening tests, laboratory tests, and imaging. The participants were diagnosed with possible or probable AD according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR, American Psychiatric Association, 2000) and National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA; McKhann et al., 2011) criteria. The diagnostic work-up included complete blood cell count, platelet count, glycemia, triglycerides, total cholesterol and fractions, alkaline phosphatase, glutamic oxaloacetic transaminase and glutamic pyruvic transaminase, bilirubins, urea, creatinine, total proteins, calcium, free T4 levels, TSH, VDRL, dosage of B12 and folates. Cranial CT scan or MRI scan with or without spectroscopy were also applied. People with scores of 18 or above in the Mini-Mental State Examination (MMSE; Bertolucci, Brucki, Campacci, & Juliano, 1994) were included in the study. Exclusion criteria were history of other neurological disorder (also excluding cases with mixed AD and vascular dementia); history of head injury resulting in loss of consciousness for more than an hour; history of alcohol or substance abuse (based on ICD-10 criteria); and history of diagnosed major psychiatric illness or current psychological comorbidity (for example, mood disorder). Although no patient had a diagnosis of mood disorder, upon screening two patients showed depression symptoms, with scores on the GDS-15 above the cut-off of 5 (Marc, Raue, & Bruce, 2008).



These two participants were excluded from the following analyses, which were conducted with 22 participants.

## 2.2. Procedures

In order to induce a specific mood state, two success-failure manipulation (SFM) computerized paradigms, developed by Mograbi et al. (2012), were used, one based on reaction time tasks (Experiment 1) and the other on memory tasks (Experiment 2) (for a full description of the development of the tasks, see Mograbi, Brown, Brand, & Morris, 2014). Two parallel versions were developed for each type of task (see description below). The SFM paradigms are designed to set and maintain the difficulty level of the task at a constant level, by first establishing the ability of the participant and then adjusting automatically the difficulty of the trials based on this ability level or individual threshold according to the condition. In the success condition, the difficulty level was set below the participant's individual threshold, this manipulation tending to lead to a neutral mood state. In contrast, in the failure condition, the difficulty level was set above the participant individual threshold, inducing a negative mood state. Participants were not informed that levels of difficulty would be manipulated, or that a mood change was expected. Indeed, to make the procedure look more natural, each task was composed of four phases. After the four trials of the practice phase, the trials composing the next phases (titration, initial success, experimental phase) continued without any indication to the participant. The order of experiments and conditions was quasi-counterbalanced among the participants, according to the following factors: Experiment 1 or Experiment 2 first; success or failure condition first in each experiment; and version allocated for success or failure, in each experiment. More details about the procedure and the experiments can be found in Mograbi et al. (2012).

For this study, each task was followed by a 10-minute break intended to allow the participants to return to a neutral mood state and to carry-over effects. During this time, participants were allowed to rest while data were collected with the caregivers.

## 2.2.1. Experiments

### 2.2.1.1. Experiment 1 – Reaction time

In version 1 a ‘car’ appeared on the left side of the screen moving to the right, with the participants having to ‘stop’ the car as soon as it appeared by pressing the spacebar of the keyboard. In version 2 objects (e.g. ball, egg or vase) appeared to fall from the ‘top’ of the screen and participants had to ‘catch’ the object by pressing the spacebar. In both versions participants received feedback after each trial. Difficulty was manipulated by varying the object’s speed.

### 2.2.1.2. Experiment 2 – Memory

The two versions of the experiment were based around memory span tasks. For version 1, a set of ten identical objects (e.g. teapot, bucket) were shown on a computer screen and these were highlighted individually in a random sequence using a red square surround. Immediately after, participants had to point to the same objects in sequence. For version 2, a sequence of digits ranging from 0 to 9 was presented both auditorily and visually to the participants, who immediately repeated it back sequentially to the experimenter. In both versions participants received feedback after each trial. Difficulty was manipulated by varying the length of the sequence from one to ten objects/digits.

## 2.3. Measures

### 2.3.1. Background variables

Global cognitive functioning was assessed with the Mini-mental State Examination (MMSE; Bertolucci et al., 1994; Folstein, Folstein, & McHugh, 1975). To screen for levels of depression, the Geriatric Depression Scale (GDS-15; Almeida & Almeida, 1999; Yesavage et al., 1982) was used. The GDS-15 consists of 15 yes/no questions, with each item representing a common symptom of depression in older adults and being scored as absent or present. Total scale scores vary from 0 to 15, with higher scores indicating greater severity of depression. Apathy was measured using the Apathy Evaluation Scale (AES-S; Guimarães, Fialho, Carvalho, Santos, & Caramelli, 2009; Marin, Biedrzycki, & Firinciogullari, 1991). Items of the AES-S explore the participant's interests and daily activities, being rated on a 4-point Likert-type scale with the following categories: Not at All True, Slightly True, Somewhat True, and Very True. The total scores range from 18 to 72 points, with a higher total score indicating greater severity of apathy. In the current study, the questions of the GDS-15 and AES-S were read to the participants, in order to ensure good comprehension.

All the background variables were collected before the application of the experimental procedures (see table 1).

PLEASE INSERT TABLE 1 HERE

### 2.3.2. Self-reported emotion

A self-report scale was used to assess the participants' mood state before and after the mood induction. Participants were asked to rate four paired emotions (frustrated and satisfied,

disappointed and pleased) with a 5-point Likert scale: Not at all (0), a little (1), moderate (2), quite a bit (3) and extremely (4). Before and after each task of the SFM participants were asked: 'I would like to know how you are feeling right now. How [emotion] are you at this moment, from 'not at all' to 'extremely'?' Further explanation was given if needed. The negative emotions in the two pairs were scored reversely and summed with the score of the positive emotions, creating a general score ranging from 0 to 16, with higher scores indicating more positive emotion.

### 2.3.3. Anosognosia questionnaire

In order to assess the level of anosognosia before and after the mood manipulation, the participants were asked to answer six questions selected from the Anosognosia Questionnaire-Dementia (AQ-D; Almeida & Crocco, 2000; Migliorelli et al., 1995). The AQ-D was specifically designed to measure anosognosia in dementia, covering functional changes commonly found during the course of this illness. Three items were selected from the first section of the questionnaire, which assesses performance of basic and instrumental activities of daily living and the three other questions were selected from the second section, which examines changes in mood and behavior in relation to daily activities (see table 2). Scoring for each item ranges from 0 (never experiences impairment in the activity) to 3 (always experience impairments).

PLEASE INSERT TABLE 2 HERE

## 2.4. Ethical issues

The main ethical issue of the study was related to the use of a mood induction procedure. However, mood induction procedures are widely used in experimental research, giving rise to moods which are mild and short lived (Frost & Green, 1982; Isen & Gorgoglione, 1983; Martin, 1990).

All participants provided informed consent, with caregivers also giving their agreement for the patient to take part. At the end of the session participants were debriefed about the purpose of the experiments and told about the success/failure manipulation.

The project was approved by the Federal University of Rio de Janeiro (UFRJ)/ Institute of Psychiatry Ethics Committee (Research Ethics Committee number 536.634).

## 2.5. Statistical analysis

Differences in awareness of symptoms were explored with repeated-measures ANOVAs, with time (pre- / post-SFM) and condition (success / failure) as within-subject factors. For the analysis of the self-reported emotions, repeated-measures ANOVAs were also used, with time (pre- / post-SFM) and condition (success / failure) as within-subject factors. In both cases, planned pairwise comparisons followed the ANOVAs. When significant interactions for awareness of symptoms were found, Pearson's bivariate correlation were calculated between awareness change and actual performance. We performed the analyses separately for each experiment (reaction time and memory).

### 3. Results

#### 3.1. Experiment 1 – Reaction time

##### 3.1.1. Self-reported emotion

Table 3 indicates that the emotional state of the participants was similar before performing the tasks, and that the failure condition specifically induced a negative mood state. Repeated-measures ANOVA showed a significant interaction between time and condition ( $F(1, 21) = 5.92, p = .024, \eta_p^2 = .22$ ). This indicates that there were significant changes in the participant's self-report of mood depending on the type of condition. Pairwise comparisons showed that the participants rated their mood lower after the memory task in the failure condition ( $p = .008$ ), but not in the success condition ( $p = .389$ ). Additionally, after performing the task, the participants rated their mood as lower in the failure condition than in the success condition ( $p = .039$ ), but not before the task ( $p = .367$ ). There was no significant main effect of time ( $F(1, 21) = 1.42, p = .247, \eta_p^2 = .06$ ) or condition ( $F(1, 21) = .92, p = .348, \eta_p^2 = .04$ ).

PLEASE INSERT TABLE 3 HERE

##### 3.1.2. Awareness of symptoms

Figure 1 indicates that doing the tasks did not have an effect on the participants' awareness of symptoms. Repeated-measures ANOVA showed no interaction between time and condition ( $F(1, 21) = 1.72, p = .204, \eta_p^2 = .08$ ) or significant main effect of time ( $F(1, 21) = .03, p = .862, \eta_p^2 = .001$ ) or condition ( $F(1, 21) = 1.43, p = .246, \eta_p^2 = .06$ ).

PLEASE INSERT FIGURE 1 HERE

### 3.2. Experiment 2 – Memory

#### 3.2.1. Self-reported emotion

Table 4 shows that the emotional state of the participants was similar before performing the tasks and that the failure condition specifically induced a negative mood state. There was a significant interaction effect between condition and time,  $F(1, 21) = 10.95, p = .003, \eta_p^2 = .34$ . Pairwise comparisons showed that the participants rated their mood lower after the memory task in the failure condition ( $p = .002$ ), but not in the success condition ( $p = .389$ ). The participants also rated their mood lower in the failure versus the success condition after performing the task ( $p = .005$ ), but not before the task ( $p = .463$ ). There was also a significant main effect of time ( $F(1, 21) = 6.65, p = .018, \eta_p^2 = .24$ ), showing that mood is lower overall after performing the tasks, and a significant main effect of condition ( $F(1, 21) = 5.86, p = .025, \eta_p^2 = .22$ ), showing that it is lower overall in the failure condition.

PLEASE INSERT TABLE 4 HERE

#### 3.2.2. Awareness of symptoms

Figure 2 shows that awareness changed according to the task condition. There was a significant interaction effect between condition and time ( $F(1, 21) = 10.24, p = .004, \eta_p^2 = .33$ ). Paired comparisons revealed increased awareness of deficit after performing the tasks in the failure condition ( $p = .001$ ), but not in the success condition ( $p = .131$ ). Further paired comparisons showed that the participants had a similar level of awareness before performing the task in both conditions ( $p = .771$ ). There was also a significant main effect of the time on ratings of anosognosia ( $F(1, 21) = 5.65, p = .027, \eta_p^2 = .21$ ) and a significant main effect of the condition

on ratings of anosognosia ( $F(1, 21) = 10.06, p = .005, \eta_p^2 = .32$ ). A Pearson's bivariate correlation was also performed and showed a significant relationship between the change in the rating of anosognosia and the actual performance of the participants only in the failure condition ( $r = .66, p = .001$ ).

PLEASE INSERT FIGURE 2 HERE

#### 4. Discussion

The present study explored the effects of mood on the level of awareness regarding symptoms in AD patients. We experimentally induced neutral and negative mood states in patients with AD and measured the resulting changes in the level of awareness regarding cognitive and behavioral symptoms in two experiments, with reaction time and memory tasks. In both experiments, the results showed that after performing the task in the failure condition, people with AD reported a more negative mood than before performing the task. As expected, performing the tasks in the success condition led to a neutral mood state. These results confirmed the efficacy of the mood induction procedure. In addition, the AD patients showed an increase in their apparent awareness following the negative mood induction, endorsing more symptoms on the AQ-D. Nevertheless, this improvement occurred only in the memory experiment, with the level of awareness remaining unchanged in the reaction time task experiment.

These results are in line with previous findings indicating that people with AD who are more depressed show more apparent awareness (e.g., Clare et al., 2011; Harwood et al., 2000). To explain this relation, a theory suggests that depression causes only apparently more awareness because of a negative bias when reporting problems (Mograbi & Morris, 2014). However, this



theory does not seem to be able to fully explain the results of the present study. Indeed, patients with AD, despite reporting a negative mood following the mood induction procedure in both experiments, showed a greater awareness of the symptoms only when the task used in the SFM was memory-based.

An explanation for these findings might be found in the Mood Congruent/Dependent Memory theories. According to the MCM theory, the negative mood state induced by the SFM in our experiments led the participants to recall more negatively toned memories when asked about their deficits, generating a greater awareness. Following a similar idea, MDM effect might also be able to account for the results of the present study. MDM is defined as the ability to increase the recall of learned material, when the subject's emotional state is the same at the time of encoding and at the time of retrieval, regardless of the content of the material (Bower, 1981). As shown by Mograbi et al. (Mograbi et al., 2012), AD patients exhibit an implicit emotional reactivity to failure, despite a lack of explicit awareness. In other words, AD patients might be encoding events of failure when they are currently experiencing low mood. Based on the MDM theory, the AD patients who were experiencing a negative mood state during our experiment, would be expected to increase the recall of events encoded when they were already in a low mood, namely events of failure. Therefore, when asked about their deficits, participants presented a greater awareness about their own difficulties.

However, the MCM and MDM phenomena do not account for the differences between the two experiments, namely that AD patients improve their awareness of deficits when the negative mood induction procedure uses a memory task, but not when a reaction time task is used? An additional explanation might emerge from the Context-Dependent Memory (CDM) effect. CDM is defined as an increased recall of material when the context at encoding and

retrieval is the same and the context is understood as external (e.g. spatial). In the case of the present study, the context can be seen as the type of task the participant is involved in. Indeed, AD patients are constantly confronted with memory failure situations, and during these situations, they might be encoding having difficulties. So, when exposed to a similar memory failure situation (in Experiment 2), they experience an increased recall of their own difficulties, leading to an improvement of their awareness.

Our findings may have important clinical implications. Firstly, the study shows again how exposure to failure reduces mood state in AD (Mograbí, Brown, et al., 2012) and this has implications for how mood might be adversely affected in everyday life. Secondly, the greater apparent awareness of deficit following failure experience in the memory condition suggests that levels of recorded anosognosia might vary according to when in a clinical session a person has been exposed to failure, perhaps involving neuropsychological assessment. The study also underlines the importance of the context, showing that only memory-based tasks produce the specific effect and this might be consistent with everyday experience where memory difficulties produce some of the most disabling effects. Finally, studies show that lack of awareness regarding the deficits in AD seems to be protective from developing depression (Clare et al., 2012; Harwood et al., 2000) and, consistent with this, it is possible that shaping the environment of a person to reduce exposure to failure might help to retain mood state, whilst making them less aware of their deficit.

It is necessary to consider some limitations of the present study. Indeed, our small sample size may affect generalizability of the results and further studies are needed to confirm our findings. Another limitation of the study refers to the absence of a control group. Healthy controls were not used to explore the impact of mood on the level of anosognosia, because, by

definition, a healthy control group would not show the lack of awareness associated with dementia. The current study was also limited to a degree by the methodology used to assess the participants' awareness. Indeed, the same questions were used to assess awareness before and after all the conditions. As pointed by Marcel et al. (2004), patients with plegia following stroke may learn how to respond to awareness measures when the questions are repeated. Nevertheless, the present study was conducted with people with dementia and the order of experiments and conditions was quasi-counterbalanced among the participants. In addition, changes in awareness were observed only after the failure memory task, suggesting that the results cannot be simply explained by practice effects.

To the best of our knowledge, this is the first study exploring in an experimental design the relation between mood state and awareness in patients with AD. As most of the studies highlighted, the existence of a relation between anosognosia and mood state is now well accepted. However, the direction of this relation is still debated in the literature. One theory is that the awareness of the deficits leads to a higher negative mood state, through a reactive depression phenomenon. Another theory suggests that depression leads to report more difficulties overall. The results of the present study support the notion that negative mood leads to a greater awareness of the deficits, and the best explanatory model is to be found in the Mood Congruent Memory and Mood/Context Dependent Memory phenomena. Further investigations of the relation between mood and awareness are needed with larger samples and the inclusion of other methodology, such as neuroimaging.

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**Table 1 – Sample characteristics**

Variable	AD group (n=22) Mean (SD)
Age	78.1 (5.6)
Gender*	17 / 5
Years of education	8.1 (4.2)
MMSE	21.5 (3.1)
AES	35.7 (6.1)
GDS-15	2.5 (1.2)

\* # female/ male

**Table 2 – Anosognosia questionnaire**

	Never	Sometimes	Often	Always
<b>1. Do you have problems remembering the date?</b>	0	1	2	3
<b>2. Do you have problems remembering where you leave things in your home?</b>	0	1	2	3
<b>3. Do you have problems remembering appointments?</b>	0	1	2	3
<b>4. Are you more rigid in your decisions, with less capacity to adapt to new situations?</b>	0	1	2	3
<b>5. Are you more irritated? Do you easily lose your temper?</b>	0	1	2	3
<b>6. Do you feel more depressed?</b>	0	1	2	3



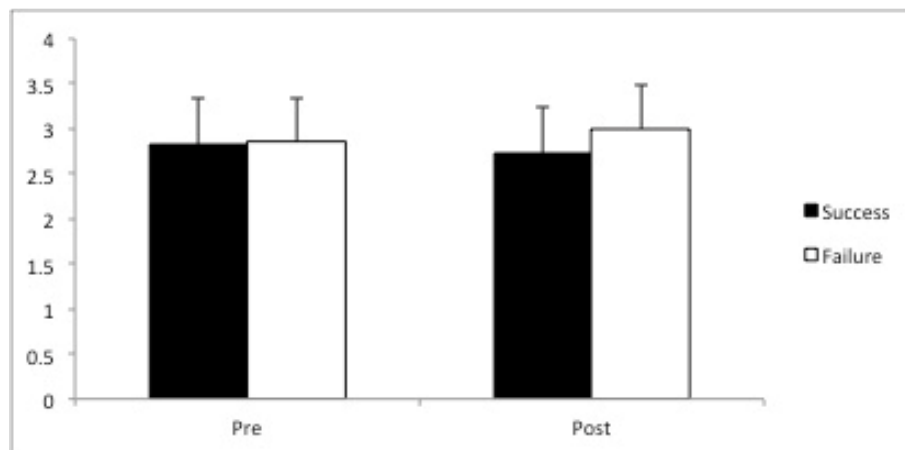
**Table 3 – Self-reported emotion before and after the SFM for the success and failure condition in Experiment 1 (reaction time)**

	Success task Mean (SD)	Failure task Mean (SD)
Pre-SFM	12.09 (1.69)	12.36 (1.56)
Post-SFM	12.36 (1.89)	11.64 (1.87)

**Table 4 – Self-reported emotion before and after the SFM for the success and failure condition in Experiment 2 (memory)**

	Success task Mean (SD)	Failure task Mean (SD)
Pre-SFM	12.27 (1.52)	12.45 (1.71)
Post-SFM	12.55 (1.74)	10.86 (2.57)

**Figure 1 – Awareness of symptoms during experiment 1**



**Figure 2 – Awareness of symptoms during experiment 2**

